

Optimized Patient-Specific Catheter Placement for Convection-Enhanced Nanoparticle Delivery in Recurrent Glioblastoma

Citation for published version (APA):

Wu, C., Hormuth, D. A., Christenson, C., Woodall, R. T., Abdelmalik, M. R. A., Phillips, W. T., Hughes, T. J. R., Brenner, A. J., & Yankeelov, T. E. (2023). Optimized Patient-Specific Catheter Placement for Convection-Enhanced Nanoparticle Delivery in Recurrent Glioblastoma. In *SC-W '23: Proceedings of the SC '23 Workshops of The International Conference on High Performance Computing, Network, Storage, and Analysis* (pp. 119-120). Association for Computing Machinery, Inc. <https://doi.org/10.1145/3624062.3624079>

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DOI:
[10.1145/3624062.3624079](https://doi.org/10.1145/3624062.3624079)

Document status and date:
Published: 12/11/2023

Document Version:
Publisher's PDF, also known as Version of Record (includes final page, issue and volume numbers)

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
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KEYWORDS

Image-guide modeling, Computational fluid dynamics, patient-specific optimization, radioactive nanoparticle, MRI, SPECT/CT

ACM Reference Format:

Chengyue, Wu, David, A., Hormuth Ii, Chase, Christenson, Ryan, T., Woodall, Michael, R. A., Abdelmalik, William, T., Phillips, Thomas, J. R., Hughes, Andrew, J., Brenner, and Thomas, E., Yankeelov. 2023. Optimized Patient-Specific Catheter Placement for Convection-Enhanced Nanoparticle Delivery in Recurrent Glioblastoma. In *Workshops of The International Conference on High Performance Computing, Network, Storage, and Analysis (SC-W 2023)*, November 12–17, 2023, Denver, CO, USA. ACM, New York, NY, USA, 2 pages. <https://doi.org/10.1145/3624062.3624079>

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SC-W 2023, November 12–17, 2023, Denver, CO, USA
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ACM ISBN 979-8-4007-0785-8/23/11.
<https://doi.org/10.1145/3624062.3624079>

1 INTRODUCTION

Glioblastoma multiforme (GBM) is the most common and deadliest of all primary brain cancers. One promising treatment strategy for patients with recurrent GBM is convection-enhanced delivery (CED) of Rhenium-186 (^{186}Re)-nanoliposomes (RNL) to provide delivery of large, localized doses of radiation. The success of treatment by CED relies on proper catheter placement for therapy delivery to maximize tumor coverage and minimize the leakage to healthy tissue. In this project, we are developing an image-guided physics-based model to optimize catheter placement for RNL delivery on a patient-specific basis.

2 METHODS

The mathematical model consists of 1) the steady-state flow field generated via the catheter infusion and the Darcy flow through the 3D brain domain, 2) the transport of RNL governed by an advection-diffusion equation, and 3) the point-spread function to transform the RNL distribution into the SPECT signal. Pre-delivery MRIs were used to assign patient-specific tissue geometries. Two scenarios were performed to personalize the model parameters: a) patient-specific calibration with longitudinal SPECT images monitoring RNL distributions, and b) population-based assignment with the leave-one-out cross-validation (LOOCV). The accuracy of model

predictions was evaluated by the concordance correlation coefficients (CCC) between predicted and measured voxel-wise SPECT signals. Furthermore, in each patient, we used the image-guided model—with either calibrated or assigned parameters—to simulate RNL distributions for all possible locations of catheter tip(s), resulting in a ratio of the cumulative dose of RNL outside the tumor to that within the tumor, termed as “off-target ratio” (*OTR*). We minimized the *OTR* to optimize the placement of catheter(s), and compared *OTRs* obtained by the optimized and the original placements.

3 RESULTS

Fifteen patients with recurrent GBM from a Phase I/II clinical trial of RNL were included in the study. For scenario a) with the patient-specific calibrated parameters, our model achieved median CCCs of 0.91, 0.87, and 0.82 for predicting RNL distributions at the mid-delivery, end-of-delivery, and 24 h post-delivery, respectively. For scenario b) with the LOOCV assigned parameters, our model achieved median CCCs of 0.89, 0.84, and 0.79 for predicting RNL distributions at the mid-delivery, end-of-delivery, and 24 h post-delivery, respectively. Compared to the original catheter placements, the optimized placements with the patient-specifically

calibrated model achieved a median (range) of 34.56% (14.70% – 61.12%) reduction on *OTR* at the 24h post-delivery. Similarly, the optimized placements with the LOOCV assigned model achieved a 34.56% (13.30% – 56.62%) reduction on *OTR* at the 24h post-delivery. Furthermore, the optimization provides insights into whether a patient is a proper candidate for CED of RNL, and whether a reduction of catheter number is possible for the patient.

4 CONCLUSION

Our image-guided model, with either patient-specific calibrated parameters or LOOCV assigned parameters, achieved high accuracy for predicting RNL distributions up to 24 h after the RNL delivery. The placement of catheter(s) optimized *via* our modeling substantially reduced the off-target ratio of RNL delivery. These results proved the potential of our image-guided modeling to guide patient-specific optimization of catheter placement for convection-enhanced delivery of radiolabeled liposomes.

ACKNOWLEDGMENTS

NCI R01CA235800, U01CA253540, and R01CA260003. CPRIT RR160005, and RP220225.